INLERNATIONAL SEARCH REPURT

anal Application No PCI/1L2004/000977

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K38/06 A61K38/07 A61K39/395 A61P35/02

C12N15/11

A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

 $\begin{array}{ll} \mbox{Minimum documentation searched (classification system followed by classification symbols)} \\ \mbox{IPC 7} & \mbox{A61K} & \mbox{A61P} & \mbox{C12N} \end{array}$

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, BIOSIS, EMBASE, Sequence Search, WPI Data

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	
X	WO 01/10383 A (VERTEX PHARMACEUTICALS INCORPORATED; GOLEC, JULIAN; CHARIFSON, PAUL; B) 15 February 2001 (2001-02-15)	1,2, 10-12, 24,25, 45-48	
Υ	see claims 1-10, table 1 and pages 50-52	1-61	
X	WO 01/94351 A (VERTEX PHARMACEUTICALS INCORPORATED; CHARRIER, JEAN-DAMIEN; BRENCHLEY,) 13 December 2001 (2001-12-13)	1,2, 10-12, 24,25, 45-48	
Υ	see claims 1,7,9 and page 50 table 6	1-61	
X	US 2003/083296 A1 (ZHANG HONG ET AL) 1 May 2003 (2003-05-01)	1,2, 10-12, 24,25, 45-48	
Υ	see claims 1 and 14-18	1-61	

X Further documents are listed in the continuation of box C.	Patent family members are listed in annex.
Special categories of cited documents: A* document defining the general state of the art which is not considered to be of particular relevance E* earlier document but published on or after the international filing date L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) O* document referring to an oral disclosure, use, exhibition or other means P* document published prior to the international filing date but later than the priority date claimed	 "T" later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family
Date of the actual completion of the International search 4 March 2005	Date of mailing of the international search report 17/03/2005
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Merckling-Ruiz, V

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	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	Relevant to claim No.		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to Claim 140.		
X	WO 99/25832 A (THE BOARD OF TRUSTEES OF LELAND STANFORD JUNIOR UNIVERSITY) 27 May 1999 (1999-05-27)	1,2, 10-12, 24,25, 45-48		
Υ	see abstract, pages 29 and 37-38	1-61		
X	WO 03/020767 A (YEDA RESEARCH AND DEVELOPMENT CO. LTD; WALLACH, DAVID; GONCHAROV, TANY) 13 March 2003 (2003-03-13) see abstract and claims	42-44		
Υ	VARFOLOMEEV E.E. ET AL.: "Targeted disruption of the mouse caspase 8 gene ablates cell death induction by the TNF receptors, Fas/Apo1, and DR3 is lethal prenatally." IMMUNITY, vol. 9, August 1998 (1998-08), pages 267-276, XP002320053 cited in the application see abstract	1-61		
Y	SALMENA L. ET AL.: "Essential role for caspase-8 in T cell homeostasis and T cell mediated immunity." GENES AND DEVELOPMENT, vol. 17, 21 March 2003 (2003-03-21), pages 883-895, XP002320054 see abstract and page 892 left column	1-61		
Y	KENNEDY N.J. ET AL.: "Caspase activation is required for T cell proliferation." J. EXP. MED., vol. 190, no. 12, 20 December 1999 (1999-12-20), pages 1891-1895, XP002320055 see abstract and pages 1894-1895	1-61		
A	CHLICHLIA K. ET AL.: "Caspase activation is required for nitric oxide-mediated CD95 (Apo1/Fas)-dependent and independent apopotosis in human neoplastic lymphoid cells." BLOOD, vol. 91, no. 11, 1 June 1998 (1998-06-01), pages 4311-4320, XP002320056 see abstract	1-61		
A	WANG J. AND LENARDO M.J.: "Roles of caspases in apoptosis, development and cytokine maturation revealed by homozygous gene deficiencies." J. CELL SCIENCE, vol. 113, 2000, pages 753-757, XP002320057 see the whole document	1-61		

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INTERNATIONAL SEARCH REPORT

'ormation on patent family members .

Inte onal Application No PCT/IL2004/000977

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 0110383	Α .	15-02-2001	AT AU DE DK EP ES JP PT SI WO US	266623 T 6894800 A 60010675 D1 1163208 T3 1163208 A2 2219381 T3 2003506389 T 1163208 T 1163208 T1 0110383 A2 2002132833 A1	15-05-2004 05-03-2001 17-06-2004 16-08-2004 19-12-2001 01-12-2004 18-02-2003 31-08-2004 31-10-2004 15-02-2001 19-09-2002
WO 0194351	Α	13-12-2001	AU CA EP JP WO US	7527901 A 2409015 A1 1289993 A1 2003535865 T 0194351 A1 2002045623 A1	17-12-2001 13-12-2001 12-03-2003 02-12-2003 13-12-2001 18-04-2002
US 2003083296	A1	01-05-2003	US AU EP JP WO	6258600 B1 2784801 A 1248858 A1 2003520052 T 0153541 A1	10-07-2001 31-07-2001 16-10-2002 02-07-2003 26-07-2001
WO 9925832	Α	27-05-1999	US AU AU CA EP JP WO	2002177565 A1 757553 B2 1699399 A 2309343 A1 1032670 A1 2001523457 T 9925832 A1	28-11-2002 27-02-2003 07-06-1999 27-05-1999 06-09-2000 27-11-2001 27-05-1999
WO 03020767	Α	13-03-2003	BR CA EP WO JP MX	0212289 A 2458985 A1 1423429 A2 03020767 A2 2005501905 T PA04002104 A	14-09-2004 13-03-2003 02-06-2004 13-03-2003 20-01-2005 07-06-2004